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Radiofrequency (RF) coil impacts the value and reproducibility of cartilage spin–spin (T2) relaxation time measurements

B.J. Dardzinski †, E. Schneider ‡§*

† Department of Radiology, Children's Hospital of Philadelphia, University of Pennsylvania, Philadelphia, PA, USA
‡ Imaging Institute, Cleveland Clinic, Cleveland, OH, USA
§ SciTrials LLC, Rocky River, OH, USA

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SUMMARY

Introduction: T2 (spin–spin) relaxation time is frequently used for compositional assessment of articular cartilage. However little is known about the influence of magnetic resonance (MR) system components on these measurements. The reproducibility and range of cartilage T2 values were evaluated using different extremity radiofrequency (RF) coils with potential differences in flip angle uniformity and signal-to-noise ratio (SNR).

Method: Ten knees underwent 3 T MR exams using RF coils with different SNR: quadrature transmit/receive (QTR); quadrature transmit/eight-channel phased-array receive (QT8PAR). Each knee was scanned twice per coil (four exams total). T2 values were calculated for the central medial and lateral femoral (cMF, cLF) and medial and lateral tibial (MT, LT) cartilage.

Results: The flip angle varied across a central 40 mm diameter region-of-interest of each coil by <1.5%. However SNR was significantly higher using QT8PAR than QTR ($P < 0.001$). T2 values for cMF (50.7 msec/45.9 msec) and MT (48.2 msec/41.6 msec) were significantly longer with QT8PAR than QTR ($P < 0.05$). T2 reproducibility was improved using QT8PAR for cMF and cLF (4.8%/5.8% and 4.1%/6.5%; $P < 0.001$), similar for LT (3.8%/3.6%; $P = 1.0$), and worse for MT (3.7%/3.3%; $P < 0.001$). T2 varied spatially, with cLF having the longest (52.0 msec) and the LT having the shortest (40.6 msec) values. All deep cartilage had significantly longer, and less variable, T2 values using QT8PAR (higher SNR; $P < 0.03$).

Conclusions: SNR varied spatially (significant) depending upon coil, but refocusing flip angle only slightly. With higher SNR, significantly longer T2 values were measured for deep (all plates) and global (MT, cMF) cartilage. T2 values varied by depth and plate, in agreement with prior studies.

Introduction

Magnetic Resonance (MR) imaging at field strengths above 1.5 T is desirable for quantitative articular cartilage morphology and composition measurements due to intrinsically higher available signal-to-noise ratio (SNR)[1,2]. While the spin–spin relaxation time, T2, is fairly constant at lower field strength[1,3–6] it decreases slightly above 1.5 T (~10% at 3 T and 10–20% at 4 T)[1,3–5,7]. This is important as T2 relaxation times have been used to evaluate the biochemical status of articular cartilage[8] in both cross-sectional and longitudinal studies of osteoarthritis and cartilage repair[9–11]. Interpretation and comparison of T2 values is challenging due to the range of acquisition parameters and analysis methods used (Table I)[3–25]. It is thus important to understand the variables, including MR system components that may influence T2 values.

The Osteoarthritis Initiative (OAI) opted to use 3 T MR systems for cartilage morphometry and T2 relaxation time measurements[26,30] on 4,794 men and women ages 45–79 who either have, or are at increased risk of developing, knee OA. These subjects were evaluated annually over 9 years with radiography and MR, along with biochemical, genetic and clinical assessments of disease activity. From baseline through the 72-month knee MR exams, the OAI used the same radiofrequency (RF) coil; for the 96-month MR exams, a new coil was used. For this reason, we investigated the impact of the coil on the value and reproducibility of cartilage T2 values by comparing measurements made at 3 T using two extremity coils with different SNR and signal reception: a quadrature transmit/receive (QTR: 0–72 months; USA Instruments, Aurora, OH, USA) and a quadrature transmit/eight-channel phased-array receive (QT8PAR: 96 months; InVivo Corp., Orlando, FL, USA)[27–29]. Quadrature-receive (QR) coils have fairly uniform SNR across the entire imaging field-of-view

* Address correspondence and reprint requests to: E. Schneider, Imaging Institute, L10 Cleveland Clinic Foundation, 9500 Euclid Avenue, HB6 Cleveland, OH 44195, USA. Tel: 1-216-444-7915; Fax: 1-216-636-1733.
E-mail address: schneie1@ccf.org (E. Schneider).

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Table I
Summary of T2 measurements at different magnetic field strengths in 'normal' cartilage in 'healthy' subjects. Mean T2 value ± SD. Global T2 values are presented; if available, top-third (T), central-third (C), and deep (D) cartilage T2 values are provided

Ref.	Field strength	Coil type	Sequence	Patellar T2 (msec)	MT T2 (msec)	LT T2 (msec)	MF T2 (msec)	LF T2 (msec)	Other T2 (msec)
Maier *et al.*[12]	1.5 T	3″ Receive	Single echo, single slice SE	20.2–40.7					
Maier *et al.*[12]	1.5 T	3″ Receive coil	MSME-SE	23.3–36.9					
Dunn *et al.*[13]	1.5 T	Four channel PA TR	Dual echo SE		32.1 ± 1.4	34.9 ± 1.8	34.9 ± 1.0	35.0 ± 1.1	
Ghosh *et al.*[14]	1.5 T	Four channel PA TR	Dual echo SE	32.1 ± 2.0	Tibial 31.1 ± 2.4		Femoral 35.1 ± 1.5		
Liess *et al.*[15]	1.5 T	8 cm circular receive surface coil	Fat-suppressed MSME-SE	23.7 ± 0.6					
Glaser *et al.*[16]	1.5 T	Quadrature	MSME-SE	32.4 ± 2.1; 36.3 ± 3.2 (T); 32.2 ± 2.4 (C); 28.8 ± 2.1 (D)					
Klosterman *et al.*[5]	1.5 T	Quadrature	MSME-SE	50.1 ± 1.5 (T); 39.7 ± 0.9 (C); 43.0 ± 1.2 (D)					
Klosterman *et al.*[5]	3 T	One channel TR	MSME-SE	52.1 ± 1.6 (T); 40.3 ± 1.2 (C); 45.2 ± 1.6 (D)					
Gold *et al.*[4]	1.5 T	Four channel TR PA	T2 prep	42.1 ± 7.05					Muscle 35.3 ± 3.85; Marrow 165 ± 4.96
Gold *et al.*[4]	3 T	Quadrature	T2 prep	36.9 ± 3.81					Muscle 31.7 ± 1.90; Marrow 133 ± 6.14
Joseph *et al.*[9]	3 T	Quadrature	MSME-SE		29.5 ± 1.8		36.8 ± 2.2		
Mosher *et al.*[10]	3 T	≥4 Channel PA receive	MSME-SE	42.4 ± 2.8 (T); 37.9 ± 2.1 (C); 35.2 ± 1.9 (D)	Tibial 47.8 ± 1.6 (T); 43.8 ± 1.8 (C); 41.5 ± 2.0 (D)		Femoral 45.6 ± 1.9 (T); 40.6 ± 1.7 (C); 38.9 ± 2.1 (D)		
Welsch *et al.*[17]	3 T	Eight channel PA receive	MSME-SE	54.2 ± 6.9					
Welsch *et al.*[17]	3 T	Eight channel PA receive	MSME-SE	54.6 ± 7.2					
Watanabe *et al.*[18]	3 T	Quadrature	MSME-SE	37.1 ± 1.9; 34.9 ± 1.0 (T); 24.2 ± 0.8 (D)					
Welsch *et al.*[19]	7 T	Quadrature	MSME-SE	54.6 ± 13.0; 58.7 ± 13.1 (T); 50.4 ± 13.5 (D)					
Welsch *et al.*[19]	7 T	Quadrature	MSME-SE		Tibial 43.6 ± 8.5; 48.1 ± 9.2 (T); 39.1 ± 9.6 (D)		Femoral 56.3 ± 15.2; 58.3 ± 14.4 (T); 54.2 ± 17.5 (D)		
Raya *et al.*[20]	7 T	28 Channel PA receive	Fat-suppressed MSME-SE	22.9 ± 4.2; 24.8 ± 4.4 (T); 20.9 ± 4.3 (D)					

(FOV) although SNR drop-off toward the edges may be found. Phased-array receive (PAR) coils have higher SNR at the edges and similar SNR at the center compared to cylindrical quadrature coils. As a result, in a PAR coil, the SNR will vary across the knee and may contribute measurement variation as a function of cartilage plate.

We hypothesized that cartilage T2 relaxation time measurement reproducibility can be improved by using the PAR coil (QT8PAR) compared to a quadrature coil (QTR). And, secondarily, that T2 times obtained with the QT8PAR coil are consistent with those obtained with the QTR coil.

Method

Study participants

The study was performed at two centers (Ohio State University and Memorial Hospital of Rhode Island) as part of an OAI pilot study[28]. The study protocol, amendments, and informed-consent documentation were reviewed and approved by the local institutional review boards.

Ten adult subjects (three men, seven women; five healthy, five with a clinical diagnosis of OA) underwent test–retest MR imaging of either their left or right knee, and two subjects (one healthy, one with OA) underwent imaging of both their right and left knees. In total, 12 knees were examined four times each. All participants were recruited for other OAI pilot MR studies[28]. Seven of the 10 subjects also participated in the OAI[30] and underwent bilateral fixed-flexion posterior–anterior (P/A) radiography[31].

MR acquisition

Test–retest images were acquired on 3 T MR systems (Siemens Magnetom Trio, Erlangen, Germany) using both QTR and QT8PAR knee coils. Imaging was performed as in the OAI[26,28,30] including:

double-oblique coronal three-dimensional (3D) Fast Low Angle Shot with water excitation (FLASH); sagittal 3D Dual Echo in the Steady State with water excitation (DESS); and a sagittal multi-slice, multi-echo spin echo (MSME-SE) acquisition for T2 relaxation time measurement. The MSME-SE acquisition (Fig. 1) used a 120 mm FOV, 3 mm slice thickness, with in-plane spatial resolution 0.31 mm × 0.45 mm, one average, 2700 msec repetition time, 7 echoes (10, 20, 30, 40, 50, 60, 70 msec) and was prescribed sagittal to the joint, co-planar with the DESS acquisition and orthogonal to the FLASH.

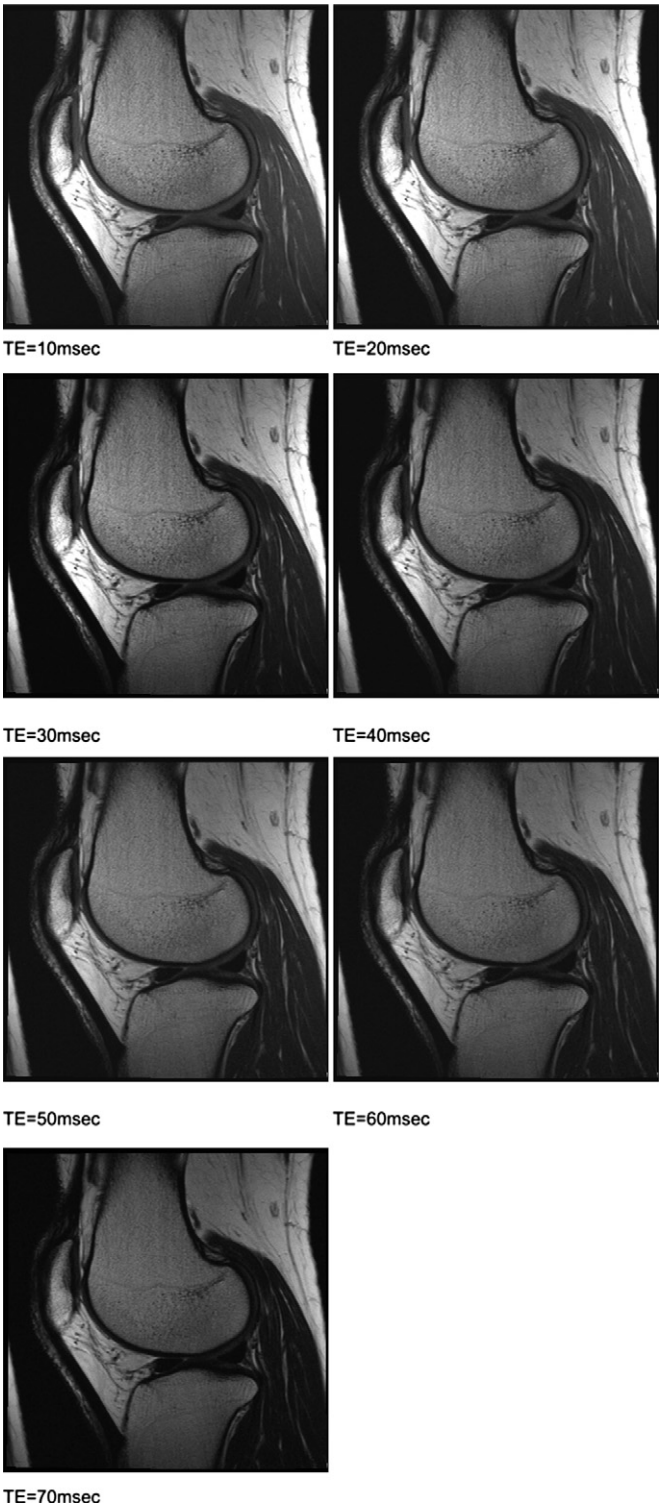

Fig. 1. Source MSME-SE images through the mid-point of the medial knee acquired using the QTR knee coil. Multiple contrast acquisitions having progressively longer TEs are combined to calculate T2 maps of the articular cartilage and adjacent tissues. These seven images illustrate how changing the TE affects the relative signal and relative contrast among the different tissues in the knee.

The coils were positioned 60 mm right/left off the magnet isocenter. Subjects were positioned feet first and supine, with the inferior end of the patella located at coil isocenter[26,28,30]. For the QTR coil, the knee was slightly flexed (about 10°), with a cushion placed beneath the knee, and the heel positioned directly on the table. The knee angle on the QT8PAR coil was fixed, also at about 10°. With both coils the foot was secured in a vertical position with the great toe pointed straight up. To reduce misalignment between exams, the knee and foot position as well as the prescription was standardized. The DESS and MSME exams utilized identical angulation and center position[26,28,30].

The OAI knee phantom has two compartments, an outer cylinder with outer diameter and length 125 mm and 128 mm and an inner sphere with 57 mm diameter. Each compartment contains a different concentration Magnevist (Schering AG, Germany) solution (sphere 10 mM; cylinder 3.33 mM) corresponding to the approximate T2 values of the deep and top layers of normal cartilage (18 msec and 50 msec, respectively)[32]. The OAI knee phantom was evaluated four times in the left and four times in the right coil position both for T2 value as well as for transmit uniformity using both RF coils (16 total exams).

Each subject underwent four MR exams. On one day, a test–retest examination was performed using one of the coils. Between the two exams the participant was removed from the magnet and allowed to walk for about 10 min. On another day, within 1 month of the first MR exam, the same acquisitions were repeated using the other coil. The order of coil use was randomized. All MR images were reviewed for image quality by the MR technologist and were immediately reacquired if unacceptable (orientation, incomplete anatomical coverage, motion, artifact, *etc.*).

T2 analysis and region selection

Since our purpose was to evaluate the system variables that affect cartilage T2, we eliminated knee compartments with visible signs of damaged cartilage. This approach improved the likelihood that a single exponential fit can assess the biological status of cartilage[23,33] using clinical acquisitions. We focused on knees with cartilage having 'normal' appearance and three or more pixels (≥1 mm) across the cartilage thickness. Visually intact surfaces on the DESS, FLASH and MSME-SE images without extreme thinning of cartilage were classified as 'normal,' although knees were not eliminated for having meniscal degeneration or tears and/or posterior or anterior cruciate ligament tears. Knees with one 'damaged' compartment (usually the patello-femoral joint) were eligible for analysis of the other two compartments; those knees having two or more 'damaged' compartments were ineligible for analysis.

T2 relaxation times were computed pixel-by-pixel from the MSME series using custom software (IDL, Exelis Visual Information Solutions, Boulder, CO). First, a threshold was manually determined (~10% of maximum signal intensity (SI)) and applied to remove the background noise. Next, a linear (two-point) fit to the log of the signal decay from the last six (of seven) echo images (Fig. 1) was performed. The goodness of fit was evaluated using a residual map (T2 fit errors on a pixel-by-pixel basis) (Fig. 2). A better fit has residual values closer to zero (darker gray scale and black pixels). Long T2 valued tissues, such as fluid, are expected to have poorer fits due to the limited range of echo times (TEs). Likewise regions of damaged cartilage might also be poorly represented by a single exponential fit[23,33].

To limit the center-to-edge variability of SNR caused by a PA receive coil[27,29], we focused on the central three slices of the lateral and medial femoral-tibial cartilage that were not covered by the

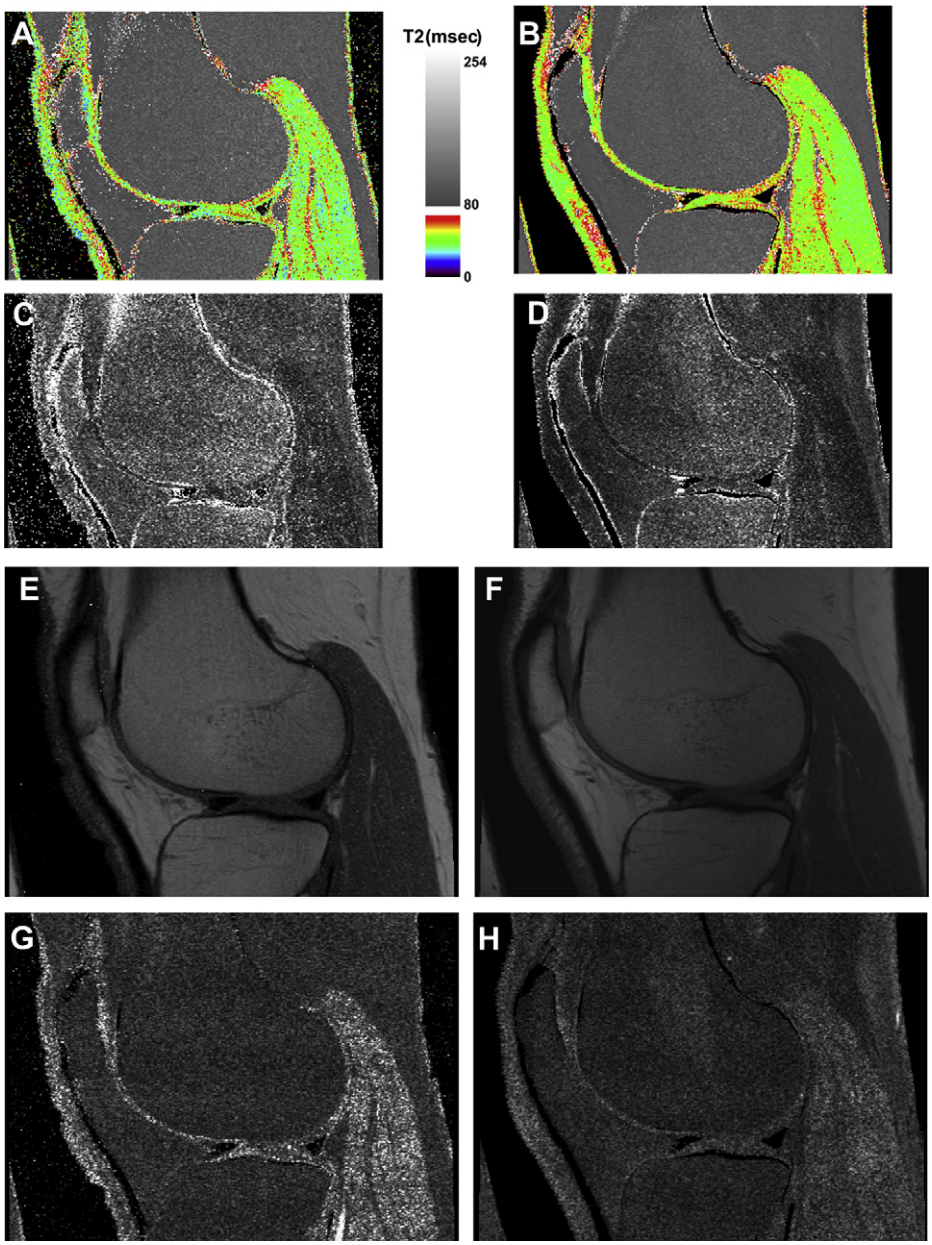

Fig. 2. Example of T2 and Mo fits and the respective residual (error) maps from the QTR coil (A) T2 map, (C) T2 error map, (E) Mo map and (G) Mo error map, and the QT8PAR coil (B) T2 map, (D) T2 error map, (F) Mo map and (H) Mo error map. The QTR residual (error) maps (C and G) have increased noise levels (brighter gray scale and white pixels) and more uniform noise. The QT8PAR coil residual (error) maps (D and H) have non-uniform noise, but demonstrate a better fit with residual values closer to zero (darker gray scale and black pixels). Synovial fluid has a poorer fit than cartilage due to the acquisition parameters (white near menisci). Gray scale indicates residual errors from 0 to 100%.

meniscus (anterior–posterior). This provided four regions-of-interest (ROIs), one each on the medial and lateral tibial plateaus (MT, LT) and on the medial and lateral central femoral condyles (cMF, cLF). The first analyzed lateral slice [Fig. 3(A)] was the fifth slice from the first lateral slice that contained bone. The first medial analyzed slice was the third slice from the first medial slice that contained bone. The femoral and tibial cartilage plates were analyzed using the same three slices for each side of the knee. The same anatomical slice locations were used for both coils.

Four regions (MT, LT, cMF, cLF) in each knee were defined by manual cartilage segmentation from the T2 map and intercept images (Figs. 3 and 4). A total of 192 regions were measured (two coils, 12 knees, two exams, four regions per knee). The cartilage-subchondral bone interface was determined on the T2 map [Fig. 4(A)] by the start of noise adjacent to the tibial cartilage (red arrows) and a combination of the start of the noise and the different grey scale values for the femoral cartilage (green arrows). The cartilage–joint interface was determined by the contrast changes on the intercept image [Fig. 4(B)] to either fluid or adjacent cartilage (red lines). Only the cartilage between the meniscus [between the red lines on Fig. 3(D–F)] was segmented and analyzed. Cartilage located underneath or above the meniscus was excluded.

After defining the regions, T2 relaxation profiles were generated by projecting the values on a line perpendicular to the subchondral bone[34–37]. An average T2 relaxation profile for each ROI was created; this average incorporated all the profiles from each of the three slices that were included in the analysis. All average profiles were normalized to 1.0 for thickness [0 = subchondral bone, 1 = articular surface; Fig. 4(D, E)], and divided into 20 segments for analysis. This allowed variation of the cartilage T2 measurement to

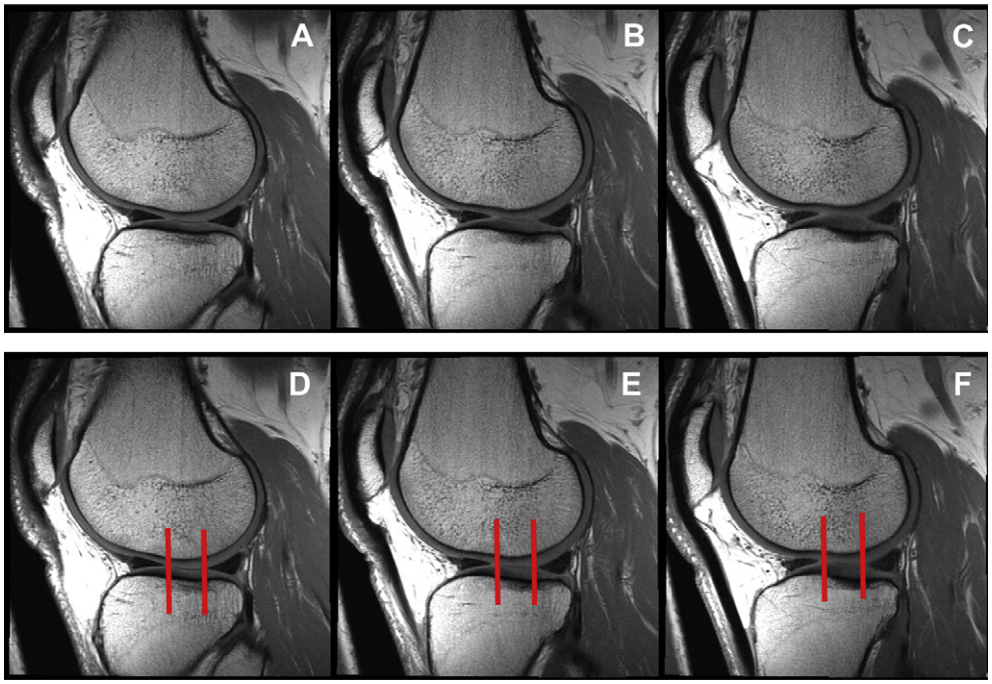

Fig. 3. Images acquired using the QT8PAR coil with TE = 10 msec. The femoral and tibial cartilage plates were analyzed on the central three slices on the medial and lateral sides of the knee. A, B, C demonstrate the central three slices of the lateral joint compartment. Only the cartilage between the meniscus (between the red lines on D, E, F) was segmented and analyzed.

be determined as a function of normalized distance from the subchondral bone. The normalized, pooled profile was analyzed after excluding the first and last four points (1–4, 17–20) to minimize the effect of partial volume and chemical shift at the subchondral bone and the synovial fluid at the articular surface [Fig. 4(D and E)]. Next, the profile for each cartilage segment was divided into three sub-regions by averaging points 5–8 (deep-third), 9–12 (central-third), and 13–16 (upper-third). The average cartilage thickness was determined from the average relaxation profile for each plate.

Three additional regions were analyzed for quality control. These regions (Fig. 5) were selected from the central medial slice and included a region in the tibial bone marrow, the infrapatellar fat pad, and the gastrocnemius. Fascial planes were avoided for the fat and muscle ROIs.

Cartilage segmentation as well as T2 value and residual calculation were performed by one person in an unpaired manner (blinded to subject identification and coil pairing). Part of cartilage segmentation included the mean thickness measurement (ThC.me). Phantom analysis was performed in a similar manner, with a 40 mm diameter ROI placed in the central compartment.

SNR measurement

To understand the influence of SNR on T2 values, SIs in cartilage and bone marrow ROIs and noise levels of two ROIs were measured for both the medial and lateral sides (Fig. 5). The bone marrow ROI spanned the entire proximal epiphysis. The cartilage ROI was as described. The noise ROI was outside the knee below the patella. To magnify the differences between the coils, the SI and noise were measured on images from the seventh echo (TE 70 msec; Fig. 1). The measurements from the test–retest acquisitions were used to compute the average SNR level for each coil.

Statistics and computation of CVs

Bland–Altman plots of test–retest differences for T2 values measured using each coil were visually assessed for variance to mean relationships and out-of-bounds measures. Differences between the values measured using QTR and QT8PAR were tested for statistical significance using a paired Student's *t*-test (null hypothesis of no difference in T2 between coils). Re-measurement reproducibility was analyzed by the root-mean-square coefficient-of-variation (RMS CV%) defined by Gluer *et al.*[38].

Results

Subjects

The 10 participants had mean age 52.2 years (range: 45–73 years) with mean body mass index (BMI) 28.2 kg/m^2 (range: 21.8–34.6 kg/m^2). Of the seven subjects who underwent bilateral knee radiography; five subjects had Kellgren–Lawrence grade (KLG) 1 knees, one knee had KLG 2, and one knee had KLG 3, using the screening, site radiograph interpretation. Both the KLG 2 and 3 knees had two or more compartments with MR evidence of cartilage abnormalities or thickness <3 pixels. Thus, only ten femorotibial joints from 10 participants were evaluated.

SNR

Each cartilage region had 470–2,237 pixels. There was a minimum of 300,000 pixels in each quality control region. The SNR (Table II) was significantly higher using QT8PAR for all cartilage, muscle, infrapatellar fat, and marrow ROIs measured on the last echo images (TE = 70 msec).

Phantoms

The mean ± standard deviation (SD) T2 values were not statistically different (internal sphere) 18.62 ± 0.12 msec and 18.79 ± 0.25 msec (P = 0.33) and (external cylinder) 52.39 ± 0.83 msec and 51.59 ± 0.78 msec (P = 0.06) using QTR and QT8PAR. The SNR over these ROIs were statistically different (sphere) 47.8 ± 1.4 and 52.7 ± 2.1 (P < 0.001) and (cylinder)

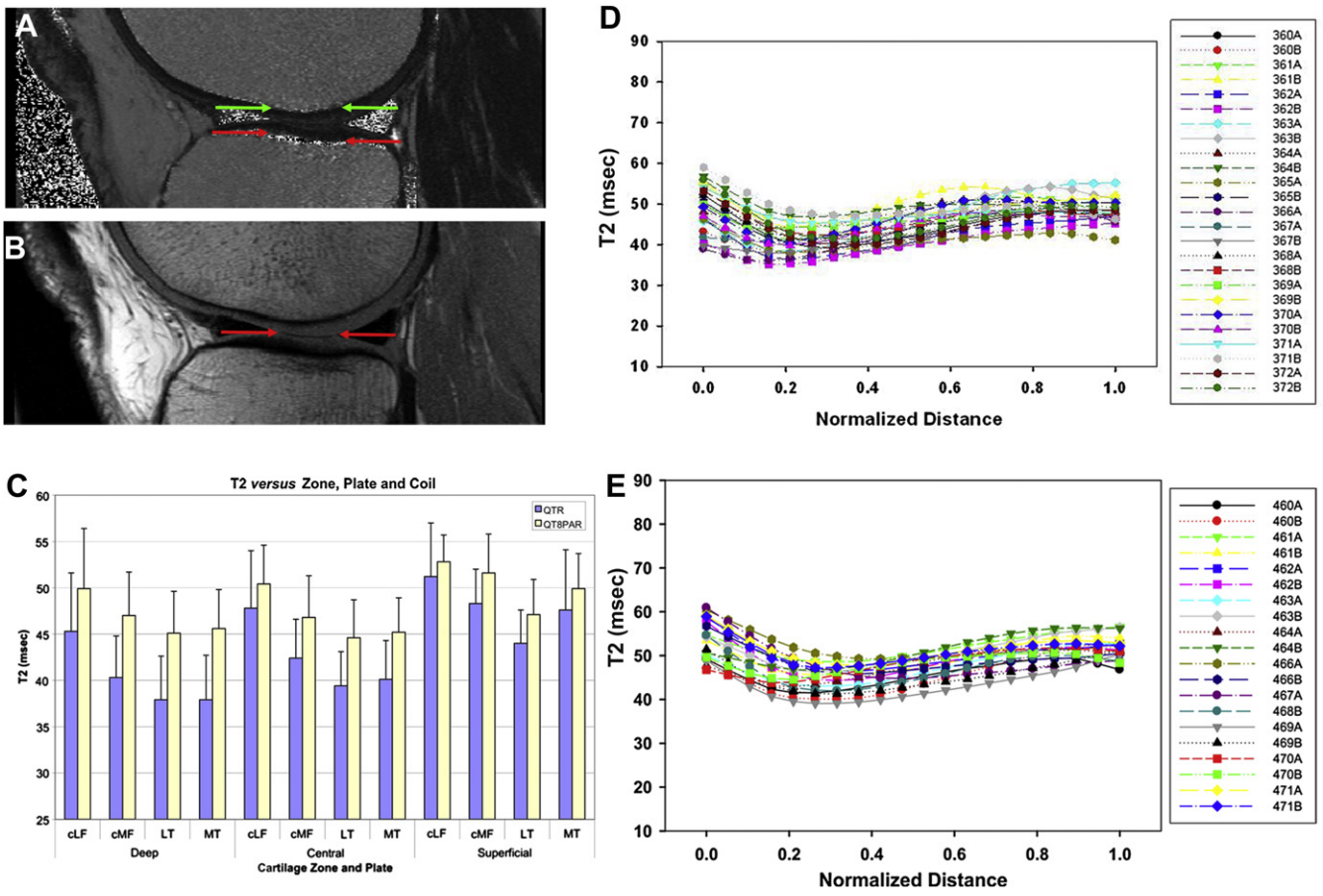

Fig. 4. The cartilage–bone interface was determined using the calculated T2 image (A) by the adjacent noise caused by the cortical bone (note the femoral cortical bone contains a narrower noise band because the tibial cortical bone also contains the chemical shift artifact signal void). The interface was determined by the start of noise adjacent to the cartilage (see red arrows for tibial cartilage and green arrows for femoral cartilage). The cartilage-joint fluid or cartilage–cartilage interface was determined using the intercept image (B) by the contrast change from cartilage to either fluid or adjacent cartilage (see red lines at the cartilage–cartilage interface). Average T2 profiles normalized to 1.0 for thickness (0 = subchondral bone, 1 = articular surface) for the cMF cartilage plate using the (C) T2 value as a function of cartilage depth, plate and RF coil (D) QTR and (E) QT8PAR coils.

111.1 ± 4.4 and 139.0 ± 13.8 ($P < 0.001$) for QTR and QT8PAR, respectively. The RF transmit uniformity (measured using a 720° pulse) was evaluated over a central 40 mm diameter spherical ROI with <10° variation (<1.5%). For a series of eight 180° refocusing pulses, this corresponds to a 0.4% signal loss. No *in vivo* RF transmit maps were made; no correction for non-uniformity was attempted in the T2 analyses. The phantom T2 values were comparable between the two sites[32].

Cartilage T2 relaxation time

Bland–Altman plots of the test–retest T2 values (not shown) were unremarkable. The T2 relaxation times and measurement reproducibility are shown in Table III [Fig. 4(C)]. The global T2 values for cMF and MT as well as muscle were significantly longer with QT8PAR ($P < 0.0004$). Due to the small number of knees, there was no significant difference in global T2 value between the coils

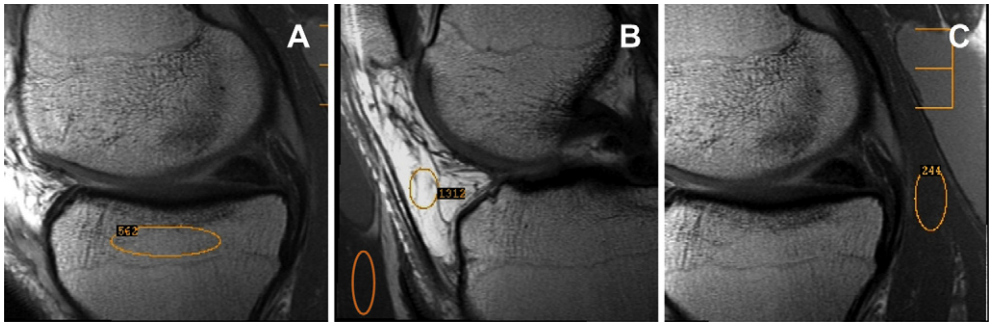

Fig. 5. Three additional ROIs were analyzed for purposes of quality control. These ROIs were selected from the most central medial slice and included a region in the tibial bone marrow (A), the infrapatellar fat pad (B), and in the gastrocnemius muscle (C). Fascial planes were avoided if possible for the fat and muscle ROIs. SNR was calculated based on the noise ROI located near the infrapatellar fat in (B).

Table II
Mean and SD (±) for SNR for bone marrow and cartilage of the MT and LT from last echo (TE = 70 msec). *P*-values assess the difference between the mean SNR levels from the two RF coils

SNR	MT marrow	MT cartilage	LT marrow	LT cartilage
QTR Coil				
Mean ± SD	33.3 ± 6.4	2.8 ± 0.7	32.4 ± 5.5	2.5 ± 0.3
QT8PAR Coil				
Mean ± SD	42.6 ± 8.1	5.6 ± 0.6	47.4 ± 8.4	6.0 ± 0.6
P-value	0.03	<0.001	<0.001	<0.001

for cLF ($P = 0.06$); LT ($P = 1.0$) and bone marrow ($P = 0.77$) global T2 values were equivalent. The T2 residual plots (Fig. 2) indicate a better single exponential fit was achieved (smaller error) using images acquired with QT8PAR (visual assessment).

The T2 reproducibility was better for cLF, cMF, and infrapatellar fat using QT8PAR. The T2 reproducibility was slightly better for LT, MT, and marrow using QTR. For muscle regions, the RMS CV% was the same in both coils [Table III(A)].

When the cartilage ROIs were divided into three depths (lower-third, central, upper-third), the T2 value increased from the subchondral bone to the articular surface for all cartilage plates and for both coils [Table III(B) and Fig. 4(C)]. For the deep layer, T2 measurements made using QT8PAR were significantly longer ($P < 0.026$) for all cartilage plates (cLF, cMF, LT, MT). The RMS CV% for the deep layer was smaller using QT8PAR for all cartilage plates except MT. For cartilage in the central-third, T2 measurements made using QT8PAR were significantly longer for cMF, LT and MT ($P < 0.003$). The reproducibility for cartilage T2 in the central-third was smaller for cLF and MT using QT8PAR and for cMF and LT using QTR. For cartilage in the top layer, only cMF and LT had significantly longer T2 times using QT8PAR ($P = 0.012$ and $P = 0.012$). The reproducibility trend was the same as for the central cartilage.

No differences between sites were noted for any analyses.

Cartilage thickness

The mean cartilage thickness was 1.6 ± 0.3 mm, 2.1 ± 0.3 mm, and 1.8 ± 0.3 mm for LT, MT and weight-bearing femoral cartilage (cLF and cMF combined), respectively. There were no statistically significant differences between thickness measurements from QT8PAR and QTR ($P > 0.2$; data not shown).

Discussion

MR imaging of cartilage is challenging because it is quite thin and has a curved surface; the longitudinal quantification of its biochemical changes utilizing relaxation time measurements thus places increased demands on MR imaging practice and technology. We explored the impact of two extremity coils with different SNR characteristics on T2 measurements of knee cartilage at 3 T. Ten middle-aged knees with relatively healthy cartilage were analyzed after test–retest imaging with both a quadrature and a PA knee coil (four measurements). All femoro-tibial compartments included in

Table III
Mean and SD (±) for T2 relaxation times and RMS CV%. *P*-values are shown for differences between the mean T2 relaxation times from the two RF coils

(A) Global T2 values for all ROIs.

T2	cLF cartilage	cMF cartilage	LT cartilage	MT cartilage	MT marrow	Fat	Muscle
QTR Coil							
Mean ± SD (msec)	49.2 ± 5.2	45.9 ± 3.8	40.6 ± 3.5	41.6 ± 3.0	106.4 ± 2.6	97.0 ± 6.5	37.9 ± 2.1
RMS CV (%)	6.5	5.8	3.6	3.3	1.0	4.4	2.9
QT8PAR Coil							
Mean ± SD (msec)	52.0 ± 3.8	50.7 ± 3.9	40.6 ± 3.8	48.2 ± 3.0	106.1 ± 3.8	94.4 ± 5.0	40.7 ± 2.4
RMS CV (%)	4.1	4.8	3.8	3.7	1.7	3.6	2.9
P-value	0.06	0.0003	1.0	0.0001	0.77	0.16	0.0004

(B) T2 values as a function of depth (deep-, central-, top-third) for all cartilage plates.

	cLF cartilage	cMF cartilage	LT cartilage	MT cartilage
T2 deep-third				
QTR coil				
Mean ± SD (msec)	45.3 ± 6.3	40.3 ± 4.5	37.9 ± 4.7	37.9 ± 4.8
RMS CV (%)	12.4	5.6	6.2	4.0
QT8PAR coil				
Mean ± SD (msec)	49.9 ± 6.5	47.0 ± 4.7	45.1 ± 4.5	45.6 ± 4.2
RMS CV (%)	4.0	5.2	4.4	5.0
P-value	0.03	0.0001	0.0001	0.0001
T2 central-third				
QTR coil				
Mean ± SD (msec)	47.8 ± 6.2	42.4 ± 4.2	39.4 ± 3.7	40.1 ± 4.2
RMS CV (%)	9.4	4.9	5.8	8.3
QT8PAR coil				
Mean ± SD (msec)	50.4 ± 4.2	46.8 ± 4.5	44.6 ± 4.1	45.2 ± 3.7
RMS CV (%)	3.9	7.0	5.2	3.3
P-value	0.13	0.003	0.0002	0.0002
T2 top-third				
QTR coil				
Mean ± SD (msec)	51.2 ± 5.8	48.3 ± 3.7	44.0 ± 3.6	47.6 ± 6.5
RMS CV (%)	5.5	5.2	4.7	9.8
QT8PAR coil				
Mean ± SD (msec)	52.8 ± 2.9	51.6 ± 4.2	47.1 ± 3.8	49.9 ± 3.8
RMS CV (%)	4.6	6.2	5.5	3.6
P-value	0.28	0.01	0.01	0.18

the analysis did not have any MR visible cartilage defects or significant thinning.

A key factor that might alter T2 value is the RF coil transmit uniformity. Transmit uniformity is influenced by coil design (both had QT), but also by patient electrical loading of the coil. In a phantom, no difference in a central 40 mm diameter spherical ROI was found in transmit flip angle. No significant difference in phantom T2 value was found for this same region. In volunteers with visibly healthy cartilage, the cMF and MT cartilage and muscle T2 values were significantly ($P < 0.003$) longer using QT8PAR. Deep cartilage had the largest change in T2 value (4.6–7.2 msec). Significantly ($P < 0.03$) higher SNR for all cartilage and marrow ROIs were found with QT8PAR. The impact of increased SNR was previously found[28] to result in measurement of increased cartilage volume (VC) with QT8PAR. Here, higher SNR levels did not significantly change cartilage thickness, but were found to increase T2 values [Table III(A)], however the extent and significance of the increase was not consistent for all cartilage plates and depths. Smaller fit residuals were found (Fig. 2) and smaller error bars were obtained on the profile plots using QT8PAR, indicating better fits were obtained with higher SNR.

Lower T2 RMS CV% were found for MT, LT, and marrow using QT8PAR. Overall we measured 3.7–11.1% RMS CV% with QTR and 3.3–6.5% with QT8PAR, lower than most prior 3 T reproducibility measurements (Table IV) and most similar to that of Stahl *et al.*[11] using one MR system and better than achieved by Mosher *et al.*[10] using five MR systems. In our study, the T2 variability was limited to patient positioning, SNR, RF coil loading, MR system variability, reproducibility of cartilage segmentation and ROI selection.

A summary of T2 test-retest reproducibility is presented in Table IV for 'normal' knee cartilage[10,14–17,19,20,36,39], most studies had a small number of subjects and/or analyzed only the patellar cartilage. Significantly intra- and inter-session reproducibility improvements were achieved by using a positioning device[36,39]. Comparison between T2 values of osteoarthritic patients and age/gender controls at 3 T were performed by two groups: Stahl *et al.*[11] used a dual-echo fast-spin-echo (FSE) T2 measurement with relatively low in-plane spatial resolution ($0.625 \times 0.625 \times 3$ mm^3), had <3% CV% reproducibility, and found systematically longer T2 values for all cartilage plates in the OA group, but reached statistical significance only in pLF (eight OA and 10 control subjects). The American College of Radiology Imaging Network (ACRIN) multicenter trial[10] found improved reproducibility as the knee cartilage quality and quantity diminished. Based on four test–retest exams in 50 subjects, they also found systematic increasing T2 values for all cartilage depths and plates between normal, mild and moderate OA; however significance was only reached between the normal and moderate groups at all depths for cLF, cMF, and patellar cartilage, and between mild and moderate groups for all depths of the patella and for cMF and cLF deep- and central-layers.

In addition to differing sensitivities to SNR levels, the four cartilage ROIs also had significantly different global T2 values: varying from 40.6 msec (LT) to 49.2 msec (cLF) with QTR and 40.6 msec (LT) to 52.0 msec (cLF) with QT8PAR. Our cartilage T2 values

Table IV
Summary of T2 test–retest reproducibility at different magnetic field strengths in 'normal' cartilage in 'healthy' subjects. Global T2 value reproducibility is presented; if available, upper layer (T), central (C), and deep (D) cartilage T2 values are provided

Ref.	Cartilage plate	Field strength	Coil type	Sequence	RMS CV%
Ghosh *et al.*[14]	Femoral	1.5 T	Four channel PA TR	Dual SE	1.5%
Ghosh *et al.*[14]	Tibial	1.5 T	Four channel PA TR	Dual SE	2.0%
Ghosh *et al.*[14]	Patellar	1.5 T	Four channel PA TR	Dual SE	4.4%
Liess *et al.*[15]	Patella	1.5 T	8 cm circularly polarized receive surface coil	Fat-suppressed MSME-SE	1.7% (average CV%)
Glaser *et al.*[16]	Patella	1.5 T	Quadrature	MSME-SE	3.2%
					3.9% (D)
					3.9% (C)
					4.7% (T)
Welsch *et al.*[17]	Talar trochlea	3 T	Eight channel PA receive	MSME-SE	3.2%
Welsch *et al.*[17]	Inferior tibia	3 T	Eight channel PA receive	MSME-SE	4.7%
Mosher *et al.*[36]	Femoral tibial	3 T	Linear	MSME-SE	10–15%
Mosher *et al.*[39]	Femoral tibial	3 T	Linear	MSME-SE	1–3%
Mosher *et al.*[10]	Medial femur	3 T	≥4 Channel PA receive	MSME-SE	9.4%
					8.6% (D)
					6.2% (C)
					5.9% (T)
Mosher *et al.*[10]	Lateral femur	3 T	≥4 Channel PA receive	MSME-SE	10.9%
					7.6% (D)
					6.3% (C)
					6.0% (T)
Mosher *et al.*[10]	Medial tibia	3 T	≥4 Channel PA receive	MSME-SE	9.2%
					6.0% (D)
					5.1% (C)
					4.9% (T)
Mosher *et al.*[10]	Lateral tibia	3 T	≥4 Channel PA receive	MSME-SE	8.1%
					6.8% (D)
					6.0% (C)
					4.6% (T)
Mosher *et al.*[10]	Patella	3 T	≥4 Channel PA receive	MSME-SE	11.0%
					7.3% (D)
					6.3% (C)
					7.3% (T)
Raya *et al.*[20]	Patella	7 T	28 Channel PA receive; linear transmit	Fat-suppressed MSME-SE	5.9%
					5.9% (D)
					5.8% (T)
Welsch *et al.*[19]	Femoral tibial	7 T	Quadrature	MSME-SE	7.1%
					6.5% (D)
					7.7% (T)

[Table III(A)] were similar to that measured[17] in the ankle (54 msec) using identical hardware and MSME-SE acquisition, and were in general agreement with the ACRIN[10] results using several different manufacturers' MR systems, acquisitions, and coils.

The depth trends are similar to prior manuscripts[18,34–37] with T2 values increasing from deep-, central-, to top-third layers (subchondral bone to articular surface) for all cartilage plates and both coils [Table III(B) and Fig. 4(C)], although several recent publications found the central-third had the longest T2 values[5,10,19,20]. The deep cartilage had significantly longer T2 times with QT8PAR, however in the central-third, only cMF, LT and MT had longer T2 values, and in the top-third, only the cMF and LT had significantly longer T2 times. Since the depth variations in cartilage T2 are statistically different and also vary depending upon cartilage plate, a simple average over all cartilage plates or even a small region-of-interest cannot be used to represent the true T2 relaxation time. This is the case even when using a restricted subregion of a cartilage plate.

In addition to magnetic field strength[3–5] and orientation[40–45], image acquisition and analysis methods[3–25] are known to impact the resultant cartilage T2 value. At 1.5 T, Maier *et al.*[12] found the multi-echo multi-slice acquisition resulted in T2 values closest to the single-echo single-slice[6,22]. Similarly Pai *et al.*[25] found cartilage T2 relaxation time varied depending on sequence, and was 28 msec for SE compared to 45 msec for FSE at 3 T. Watanabe *et al.*[18] found the average T2 value measured by single-slice was longer than that measured by multi-slice. Our T2 values [Table III(A)] were longer than measured by Gold *et al.*[4] (36.9 msec patellar cartilage; 31.7 msec muscle) using a 3 T GE (General Electric Healthcare, Waukesha, WI) and QTR. In addition to changing absolute T2 times with acquisition sequence (single- vs multi-slice and SE vs FSE), the number of echoes and TE values play a role in measurement value and sensitivity to change. Some authors have used fat-suppressed imaging, others have used only a two-echo acquisition. Another confounder of absolute T2 times is analysis method: a three-point time domain or a two-point natural log fit results in different values. Likewise, including or excluding the first data point (earliest TE) will result in different values depending upon the amount of stimulated echoes present[6,12,22]. Furthermore, Koff *et al.*[21] determined that fitting algorithms can produce different T2 values; non-linear calculations resulted in the shortest T2 values, linear fits were intermediate, and noise-weighted fits resulted in the longest values. The sensitivity of analysis algorithms to low SNR[24] was found to particularly impact the shorter deep cartilage values.

Limitations of this study include the small number of knees ($n = 10$), increased variability because two sites were used for image acquisition, and only two measurements were made with each coil (Gluer *et al.*[38] advises a minimum of 14 knees measured four times). Other limitations include the visible health of the femoro-tibial cartilage: all patella-trochlea joints as well as femoral-tibial joints with cartilage damage were eliminated to enable a single exponential fit to be used for all plates. ROI selection and cartilage segmentation were both manual, which could introduce analysis errors. ROI variability may have contributed to the lack of statistically significant changes in the cLF central and upper as well as the MT upper layers of cartilage. ROIs were limited to small regions where magic angle effects and knee positioning would not dominate reproducibility[40–45] as well as to enable comparison to other studies. These results can be used as the lower limit of SNR-induced changes in T2 value over the knee. Use of the two-point time-domain fit and its known sensitivity to noise is another limitation, although this methodology was selected to amplify the impact of noise. We did not perform *in vivo* B1 mapping on each subject and coil combination. The impact of subject loading on the refocusing flip angle is unknown, although with contemporary transmit extremity coils it is expected to be much less than when using transmit body coils. Although subject foot and leg position was well defined and slice orientation standardized, a positioner was not utilized and might have served to reduce measurement variability.

Our findings of variable T2 values resulting from use of different MR system components (extremity coil) leads to question "what is the true absolute T2 value?" The system influences include magnetic field strength, refocusing pulse flip angle (coil design and patient loading), and SNR. Low SNR results in underestimated values, particularly in the deep cartilage with shorter T2 values. We have shown that SNR impacts the different ranges of T2 values variably. In practice, SNR, spatial resolution and acquisition duration are tradeoffs. Use of high SNR images (with last echo image SNR above 2) and analysis methods insensitive to noise should enable reaching the "true" T2 value asymptotically. As with all quantitative imaging, measurement and interpretation of T2 values requires reproducible measurement and analysis approaches, including consistent MR system components. Our findings further imply that evaluations should be within subject, and should include internal landmarks and reference tissues that do not change with the disease process under investigation, if possible.

In conclusion, knee articular cartilage T2 values can vary with plate and coil, with the cLF condyle having the longest value and the LT plateau having the shortest value. Under conditions of higher SNR, significantly longer T2 values were measured; this was particularly evident for the deep cartilage layer as well as the cMF. This effect is the same order of magnitude as the impact of changing magnetic field strength.

Author contributions

All authors have made substantial contributions to all three sections below:

(1) The conception and design of the study (ES), or acquisition of data (ES), or analysis (BJD) and interpretation of data (BJD and ES).
(2) Drafting the article or revising it critically for important intellectual content (BJD and ES).
(3) Final approval of the version to be submitted (BJD and ES).

ES (schneie1@ccf.org) takes responsibility for the integrity of the work as a whole, from inception to finished article.

Role of the funding source

The funding source, NIAMS, had input into the study design and data collection methods, put did not participate in these activities. All data analysis and interpretation, manuscript writing and decision to submit for publication were the sole responsibility of the authors.

Conflict of interest

BJD and ES were supported in part by a subcontract from the OAI coordinating center contract (NIAMS/NIH N01-AR-2-2258) to perform this pilot study and analysis.
ES has a fee for service contract with NIAMS as the NIAMS OAI Technical Advisor.
BJD has no conflicts pertinent to this work.

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